

# INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	(Fo	e Notification of Transmittal or rm PCT/ISA/220) as well as	of International Search Report , where applicable, item 5 below.
PU4758WO	ACTION		Discit. Date (day/month/your)
International application No.	International filing date (day/m	onth/year) (Earliest) F	Priority Date (day/month/year)
PCT/US 03/22717	21/07/20	03	23/07/2002
Applicant			
SMITHKLINE BEECHAM CORPORA	ATION		
This International Search Report has bee	n prepared by this International	Searching Authority and is t	ransmitted to the applicant
according to Article 18. A copy is being tra	ansmitted to the International Bu	reau.	
This International Search Report consists	of a total of8	sheets.	
	a copy of each prior art docume		
. Desired the second			
Basis of the report     a. With regard to the language, the	international search was carried	out on the basis of the inte	rnational application in the
language in which it was filed, un	less otherwise indicated under t	his item.	
Authority (Rule 23.1(b)).	vas carried out on the basis of a		
b. With regard to any <b>nucleotide</b> are was carried out on the basis of the		closed in the international a	pplication, the international search
	onal application in written form.	•	
filed together with the interest	ernational application in compute	er readable form.	
<u> </u>	o this Authority in written form.		
	o this Authority in computer read		ovend the disclosure in the
international application	bsequently furnished written sed as filed has been furnished.	quence listing does not go b	eyond the disclosure in the
the statement that the infurnished	formation recorded in computer	readable form is identical to	the written sequence listing has been
2. X Certain claims were for	und unsearchable (See Box I).		'
3. Unity of invention is la	cking (see Box II).		
			•
4. With regard to the <b>title</b> ,			
<u></u>	submitted by the applicant. Ished by this Authority to read as	e follows:	
the text has been estable	islied by this Adhorty to read a	, 10110443.	
5. With regard to the abstract,			
the text has been estable	submitted by the applicant. ished, according to Rule 38.2(b) ne date of mailing of this interna	, by this Authority as it appe ional search report, submit	ars in Box III. The applicant may, comments to this Authority.
6. The figure of the drawings to be pu			
as suggested by the app			None of the figures.
because the applicant fa	ailed to suggest a figure.		
because this figure bette	er characterizes the invention.		

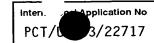


Intern	l application No		
PCT/US	03/22717		

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present	t invention relates cularly to pyrazolop	to inhibitors of tyrimidine compound	the kinases GSK3 c ls useful as kinas	or TIE2, and e inhibitors.
				·
		·		

## INTERN. ONAL SEARCH REPORT



A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/519 A61P3/06 A61P17/14 A61P15/08

A61P5/48 A61P9/10 A61P35/00 A61P25/28

A61P9/12 A61P37/04

A61P43/00 According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

 $\label{lower model} \begin{array}{ll} \mbox{Minimum documentation searched (classification system followed by classification symbols)} \\ \mbox{IPC 7} & \mbox{A61K} \end{array}$ 

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

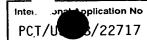
EPO-Internal, CHEM ABS Data, WPI Data

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
А	WO 00 38675 A (HOLDER JULIE CAROLINE; SMITH DAVID GLYNN (GB); COGHLAN MATTHEW PAU) 6 July 2000 (2000-07-06) cited in the application abstract page 1, paragraph 1 - paragraph 4 page 2, paragraph 3 page 5, paragraph 4 page 11, paragraph 3 -page 13, paragraph 2	1-20
Α	US 5 593 997 A (DOW ROBERT L ET AL) 14 January 1997 (1997-01-14) abstract column 1, paragraph 1 column 2, line 18 -column 4, line 25 column 11, paragraph 5 -column 12, paragraph 5 claims 1-16	1-20

χ Further documents are listed in the continuation of box C.	χ Patent family members are listed in annex.
Special categories of cited documents:      A' document defining the general state of the art which is not considered to be of particular relevance      E' earlier document but published on or after the international filing date      L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)      O' document referring to an oral disclosure, use, exhibition or other means      P' document published prior to the international filing date but later than the priority date claimed	<ul> <li>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</li> <li>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</li> <li>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</li> <li>"&amp;" document member of the same patent family</li> </ul>
Date of the actual completion of the international search	Date of mailing of the international search report
17 December 2003	30/12/2003
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL – 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  Fax: (+31-70) 340-3016	Authorized officer  Langer, 0

2

#### INTERN TONAL SEARCH REPORT



		PC,T/U	/22717
C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
A	WO 01 19829 A (BASF AG ;HIRST GAVIN C (US); RAFFERTY PAUL (US); RITTER KURT (US);) 22 March 2001 (2001-03-22) abstract page 7, paragraph 3 -page 8, paragraph 3 page 14 -page 18		1-20
A	WO 98 14449 A (CIBA GEIGY AG ;TRAXLER PETER (CH); BOLD GUIDO (CH); FREI JOERG (CH) 9 April 1998 (1998-04-09) abstract page 1, paragraph 1 page 5, paragraph 4 -page 6, paragraph 2		1-20
·			

2

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

#### Continuation of Box I.2

- a) Dependent claims 16-18 have been drafted as method claims but refer to use claim 14. They have been assumed to read "The use of claim 14 (...)", cf. page 8, lines 25-30.
- b) The expression "serine/threosine kinase" in claims 8 and 15 has been searched as reading "serine/threonine kinase", cf. page 3, line 18 of the description.
- c) The expression "piperadinyl" in claim 4 has been searched as reading "piperidinyl", cf. page 7, line 31 of the description.
- d) The expressions "disease or condition characterized by misregulation of a protein kinase" in claims 1, 14 and dependent claims and the further specifications of the kinase being "a serine/threosine kinase" (claims 8 and 15), "GSK3" (claims 9 and 16), "a tyrosine kinase" (claims 10 and 17), and "TIE2" (claims 11 and 18) lack clarity within the meaning of Article 6 PCT because it is unclear which specific pathological conditions (diseases) and indications do fall within this mechanistic definition and which do not.
- e) The expression "pharmaceutically acceptable derivatives" in present claims 1, 14 and dependent claims relates to compounds defined by reference to a desirable characteristic or property, namely their capability to provide "upon administration to a mammal '...! (directly or indirectly) a compound of the present invention or an active metabolite thereof" (page 11, line 30 to page 12, line 2).

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

f) Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of compounds according to formula (I) in the treatment of a pathological condition (disease) selected from the group consisting of type 2 diabetes, hyperlipidemia, obesity, CNS disorders, neurotraumatic injuries, baldness or hair loss, atherosclerotic cardiovascular disease, hypertension, polycystic ovary syndrome, ischemia, immunodeficiency and cancer or to provide immune potentiation.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international

International Application No. PCT/US 03 &2717

# FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.





Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	rnational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 1-13 and 20 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. X	Claims Nos.:  because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
	see FURTHER INFORMATION sheet PCT/ISA/210
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remai	The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

# INTERN ONAL SEARCH REPORT

Infq

n on patent family members

PCT/U 3/22717

	•				
Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0038675		06-07-2000	AU	1877700 A	31-07-2000
0000070	, .	30 2	EP	1140070 A1	10-10-2001
			WO	0038675 A1	06-07-2000
US 5593997	Α	14-01-1997	NONE		
WO 0119829		22-03-2001	AT	247657 T	15-09-2003
			AU	7495000 A	17-04-2001
			BG	106586 A	31-01-2003
			BR	0014073 A	16-07-2002
			CA	2385747 A1	22-03-2001
			CN	1390220 T	08-01-2003
			CZ	20020936 A3	16-10-2002
			DE	60004685 D1	25-09-2003
			EP	1212327 A2	12-06-2002
			JP	2003509428 T	11-03-2003
		ſ	NO	20021328 A	21-05-2002
			SK	3812002 A3	11-09-2003
			TR	200201505 T2	21-01-2003
			WO	0119829 A2	22-03-2001
			US	6660744 B1	09-12-2003
			US	2002156081 A1	24-10-2002
WO 9814449	<del>-</del>	09-04-1998	 AU	4706997 A	24-04-1998
			AU	4779897 A	24-04-1998
			WO	9814449 A1	09-04-1998
			WO	9814451 A1	09-04-1998
			ID	18494 A	16-04-1998
			ZA	9708801 A	02-04-1998